REMARKS

In view of the foregoing amendments and the following representations, reconsideration and allowance of the above-identified application is respectfully requested.

The present Amendment is in response to the Office Action mailed January 27, 2010. Upon entry of the present Amendment claims 1, 4, 15, 17-20, 23-26 and 35-41 will be pending. Claims 2 and 3 have been canceled without prejudice and the limitations of claim 3 have been incorporated into claim 1. Independent claims 1 and 35 have been amended to recite a specific embodiment of the present invention. Specifically, independent claims 1 and 35 require the controlled release core (or osmotic tablet) to comprise a core and a sustained release coating surrounding the core. The core contains at least one excipient and metformin hydrochloride as the only active pharmaceutical ingredient. Independent Claims 1 and 35 have also been amended to indicate a seal coating may optionally be present between the sustained release coating of the metformin core and the immediate release pioglitazone coating. Independent Claims 1 and 35 also require the immediate release pioglitazone hydrochloride layer to be applied to the sustained release coating (or the first seal coating if present). Claim 1 has been amended to require not less than 95% of the pioglitazone hydrochloride is released *in vitro* within 45 minutes. No new matter is added by the present amendments. Support for the sustained release coating can be found on page 7, lines 22-23 and in the Examples on pages 13-27 of the specification as filed. Support for the optional seal coating can be found on page 10, lines 7-12 and in the Examples on pages 13-27 of the specification as filed. Support for the *in vitro* release of not less than 95% of the pioglitazone hydrochloride within 45 minutes can be found on page 12, lines 8-15 of the specification as filed.

Dependent claims 4, 15, 17, 18, 20, 25 and 26 have been amended to conform to the amendments to independent claim 1.

Applicants gratefully acknowledge the withdraw of the prior rejection under 35 U.S.C. § 103(a) based upon Adjei, U.S. Patent No. 6,403,121 in view of Menon et al., The American Journal of Gastroenterology, Vol. 96, No. 5, pps. 1631-1634 (2001).

On pages 3-6 of the Office Action the Examiner rejected claims 1-4, 15, 17-20, 23-26 and 35-41 under 35 U.S.C. § 103(a) as being unpatentable over Lewis, WO 01/35940 (hereinafter "Lewis") in view of Timmins, WO 99/47128 (hereinafter "Timmins").

Reconsideration is requested in view of the present amendments and remarks.

The present claims currently recite a pharmaceutical dosage form that contains a controlled release metformin core (or osmotic tablet) comprising a core and a sustained release coating. An immediate release pioglitazone layer is applied to the outer surface of the controlled release core, which is either a sustained release coating or the optional seal coating. The dosage form also must release not less than 95% of the pioglitazone within 45 minutes during *in vitro* testing and contain less than 0.6% of the recited pioglitazone impurities. None of the cited references disclose or suggest this unique structure of a controlled release core with only one drug, metformin in the controlled release core, wherein the controlled release core further comprises a sustained release coating, and wherein an immediate release layer comprising pioglitazone is applied to the sustained release coating (or seal coating), and which further provides the recited pioglitazone rapid release and impurity profile.

As explained in the specification on page 12, during development of the presently claimed dosage form Applicants were required to overcome substantial problems. Specifically, Applicants needed to develop a dosage form that allowed pioglitazone hydrochloride to be sufficiently adhered to an outer surface of a sustained release coating thereby allowing further processing, such as packaging and shipping. The adherence also needed to allow for a quick release of the pioglitazone following administration. The competing adhesion/release problem was further complicated by the stability concerns for the pioglitazone, which tended to degrade. The Applicants discovered a solution to these problems in a unique design that combined a controlled release core comprising a metformin core surrounded by a sustained release coating, which is further coated with an immediate release layer of pioglitazone hydrochloride (with a seal coating between the sustained release coating and immediate release coating being an optional variant). This unique solution which combines an immediate release layer of pioglitazone hydrochloride applied directly to either a sustained release coating or a seal coating is not suggested by the general teachings of the cited art. Moreover, the combined teachings of the cited art would

not suggest the presently claimed invention to the skilled artisan with a reasonable expectation of obtaining a stable metformin/pioglitazone product that provides the claimed pioglitazone *in vitro* release characteristics.

Lewis, the primary reference relied upon by the Examiner, teaches an immediate release dosage form containing immediate release forms of both metformin and pioglitazone. There is no mention, disclosure or suggestion of preparing a controlled release metformin core and applying an immediate release pioglitazone layer to the core as required by the pending claims. Applicants note that the Examiner does not even contend Lewis teaches a controlled release core. *See* January 27, 2010 Office Action at 4, last paragraph. At best, Lewis teaches the metformin and pioglitazone components should be separated by a rapidly dissolving inert barrier. *See* Lewis at page 1, lines 38-39.

Timmins also does not provide guidance to the skilled artisan for preparing a controlled release core comprising a metformin core surrounded by a sustained release coating as recited in the pending claims. Timmins discloses a biphasic extended release dosage form that contains (1) a biguanide, such as metformin, employed in an inner solid particulate phase containing an extended release material and metformin in an inner core and (2) additional metformin embedded in an extended release material in the outer solid continuous phase. *See* Timmins at pages 14-15.

Because Timmins discloses controlled release matrix formulations and not controlled release cores comprising sustained release coatings, Applicants submit that the combination of Lewis and Timmins would not lead to the presently claimed invention.

Further, Timmins only briefly suggests that a thiazolidinedione, such as pioglitazone and other thiazolidinediones, can be applied to the biphasic dosage form as a "separate rapidly dissolving layer". *See* Timmins at pages 21-22. However, Timmins provides very little guidance to a skilled artisan for preparing a thiazolidinedione layer and more importantly, no guidance for preparing a pioglitazone hydrochloride layer that has good adhesion, good release and good stability characteristics when applied to a sustained release coating (or a seal coating) as recited in the pending claims.

Applicants submit that a combination of Lewis and Timmins would not result in the presently claimed invention. At best, a combination of Lewis and Timmins would result in a tri-phasic tablet, containing two sustained release metformin components and an

immediate release pioglitazone component. However, this hypothetical product would not possess the specifically recited controlled release core comprising a sustained release coating, wherein an immediate release layer of pioglitazone hydrochloride is coated onto the sustained release coating (or optionally the seal coating), and wherein the final product would provide good adhesion of the immediate release layer and good release and stability of the pioglitazone hydrochloride.

Because none of the cited references is concerned with the unique problems associated with employing an immediate release layer comprising pioglitazone hydrochloride applied to a sustained release coating (or seal coating), there are no instructions in the cited art on how to solve the specific adherence/release/stability problems Applicants have overcome while developing the present invention. Therefore, Applicants submit the currently pending claims are patentable over the cited art of record and request the above 35 U.S.C. §103(a) rejections be withdrawn.

On pages 2-3 of the Office Action the Examiner provisionally rejected claims 1-4, 15, 17-20, 23-26 and 35-41 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-50 and 55-63 of co-pending Application No. 11/093,742 (hereinafter the '742 application).

The present application was filed before the '742 application. Further, the '742 application is currently rejected under 35 U.S.C. §103(a). It is respectfully submitted that in view of the above amendments and remarks the provisional double patenting rejection will be the only remaining rejection in the present application. The withdrawal of the provisional double patenting rejection is appropriate according to MPEP § 804(I)(B)(1) which reads in relevant part as follows:

> If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier filed application to issue as a patent without a terminal disclaimer.

It is therefore requested that the above double patenting rejection be withdrawn and a notice of allowance issued. Applicants note that a similar provisional double patenting rejection was removed in the present application over co-pending U.S. Application Serial No. 11/094,493 in the Office Action dated February 26, 2009.

Based upon the foregoing amendments and representations, Applicants respectfully request that the rejection of the claims in the above-identified application be withdrawn. Early and favorable action is earnestly solicited.

The Examiner is also invited to telephone the undersigned if any further actions are required to obtain allowance.

Respectfully submitted,

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